Remarks

Claims 1-12 are pending in the application. Claims 9-12 are designated herein as withdrawn pursuant to a restriction requirement. Applicants expressly reserve their right to file one or more divisional applications with respect to any of the non-elected subject matter.

Obviousness Double-Patenting Rejection

Claims 1-8 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 15 of copending Application No. 11/567,410. The Examiner asserted that the conflicting claims are not identical but they are not patentably distinct from each other because the fluorine substituted compounds of claim 1 herein overlap with compounds claimed in the '410 application. This rejection is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Pursuant to MPEP §804,

> If a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer.

Applicants respectfully request that the Examiner withdraw the pending obviousness-type double patenting rejection upon a finding that all other rejections in the instant case have been overcome.

Claim Rejections – 35 USC §112

Claim 8 was rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 8 was also rejected under 35 USC §112, first paragraph, allegedly because the specification did not reasonably provide enablement for a combination of a compound of Claim 1 with any "one or more blood glucose-lowering active ingredients". Applicants have canceled Claim 8 by virtue of the instant amendment thereby rendering these rejections moot.

Claim Rejections – 35 USC §103

The Examiner rejected Claims 1-8 under 35 U.S.C. §103(a) as being unpatentable over Ohsumi et. al. (U.S. Patent No. 6,815,428; Of record) in view of Scarlett Goon and Carolyn R. Bertozzi (Metabolic substrate engineering as a tool for glycobiology; Glycobiology, Principles, Synthesis and Applications, Chapter 18, 2001, Pages 641-674; PTO-892) further in view of Blanchard et. al. (Chemistry & Biology, 8, 2001, 627-633; Of record).

This Office Action is non-final due to the new/modified grounds of rejection. In the previous Office Action dated 5/4/07, Claims 1-8 were rejected under 35 U.S.C. §103(a) as being unpatentable over Ohsumi et. al. (US Patent No. 6815428) in view of Blanchard et. al. (Chemistry & Biology, 8, 2001, 627-633).

In said Office Action dated 5/4/07, the Examiner stated that Blanchard et. al. discloses that the substitution of fluorine in sugar in either C2 or C5 positions can significantly slow the metabolism of glycosides. (Page 628, Column 1, Paragraph 3 to Column 2, Paragraph 1). The Examiner alleged that it would have been obvious to one of ordinary skill in the art at the time the invention was made to make and use the compound of the instant application because the compound is a structural analog of the compounds disclosed for the treatment of diabetes by Ohsumi et. al. According to the Examiner, one of ordinary skill in the art would have been motivated to make and use the instant compound (Example 9 of Applicant's application) for the treatment of diabetes because the compound is a structural analog of those disclosed in Ohsumi et. al. and the substitution of the sugar moiety with fluorine is expected to slow metabolism of the compound without sacrificing the inhibitory efficacy. The Examiner concluded that one of ordinary skill in the art would have reasonably expected that the substitution of the sugar moiety with fluorine will result in substantially similar or better pharmaceutical efficacy.

Applicants respectfully disagreed with the 5/4/07 rejection for the following reasons. Blanchard et. al. discloses glycosilation/deglycosilation reactions on ß-glycosidases. These enzymes are very different from SGLTs. The former are enzymes capable of cleaving glycosidic bonds as one step in the intestinal digestion process. SGLTs, on the other hand, are membrane transport proteins which transport sugars (i.e. glucose) across cell membranes. The function of each target enzyme is completely different.

Different enzymes have different recognition patterns for their target molecules. Blanchard et. al. discloses/suggests fluorine substitution close to the anomeric center of the sugar (i.e. C-2 or C-5 position in the sugar)(page 628, 3rd paragraph) in order to slow down or inhibit the activity of glycosidases. The compound(s) of the instant invention have a fluorine substituent in the 4-position (or 3-position) of the sugar which is the position most distant from the anomeric center. Blanchard et. al. does not teach or suggest whether or not 4-fluoro-glucose derivatives would be recognized by the target glycosidase or have the same desired effect. Therefore, one of ordinary skill in the art would not be motivated by Blanchard to conclude that substitution of fluorine in the 4- or 3-position of the sugar would yield compounds that had substantially similar or better inhibitory activity against SGLTs.

The current office action combines the previous rejections with one additional reference i.e. Scarlett Goon and Carolyn R. Bertozzi (Metabolic substrate engineering as a tool for glycobiology; Glycobiology, Principles, Synthesis and Applications, Chapter 18, 2001, Pages 641-674; PTO-892).

Applicants repeat all the arguments set forth in the response dated 11/5/07. With respect to the new/modified ground for rejection (i.e. Goon et. al.), Applicants respectfully assert that this new reference still does not provide the requisite motivation to support the modification i.e. the replacement of fluorine in the 4-position (or 3-position) of the sugar moiety. In the current office action, the Examiner states the following:

> Goon et. al. teaches the effects of halogenation on sugar moieties. Goon particularly points out the use of fluorine as the most commonly used halogen (See pages 655-659).

Indeed, Goon et. al. teaches "effects" of halogen substitution in certain sugar derivatives (none of which are structurally similar to compounds of the instant invention), but the nature of the effects cannot be generalized. Recited on page 655 is the following:

> The similar properties of the fluorine atom and hydroxyl group suggest that substitution *might* be tolerated by biosynthetic enzymes. The

introduction of a fluorohexose or hexosamine analog into a biosynthetic pathway *might* lead to metabolic *incorporation* or metabolic *disruption* (emphasis added).

When assessing the patentability of chemical analogs, the issue becomes whether the prior art suggests substituting one moiety for another with an expectation of obtaining similar properties. "[S]tructural similarity alone is not sufficient to establish obviousness." *Eli Lilly and Co. v. Zenith Goldline Pharmaceuticals, Inc.*, 2001 U.S. Dist. LEXIS 18361 at *24 (S.D. Ind. 2001). One of ordinary skill in the art cannot simply take various components and combine them without a commonality of purpose or characteristics that gives the artisan some reasonable expectation of success. "Chemical compounds present special issues of obviousness because of the limited number of elements, recurring groups or substitutes in complex molecules, the structural similarities within classes of related compounds, and the ability of chemists to undertake systematic experiments modifying known compounds." *Eli Lilly* at *14. "For a chemical compound, a prima facie case of obviousness requires 'structural similarity between claimed and prior art subject matter. . . where the prior art gives reason or motivation to make the claimed compositions'." *Yamanouchi Pharmaceutical Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000), quoting *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990) (en banc); accord, *In re Papesch*, 50 C.C.P.A. 1084, 315 F.2d 381, 391 (C. C. P. A. 1963).

Beyond looking to the prior art to determine if it suggests doing what the inventor has done, one must also consider if the art provides the required expectation of succeeding in that endeavor. See In re Dow Chem. Co., 837 F.2d at 473, 5 U.S.P.Q.2d at 1531("Both the suggestion and the expectation of success must be founded in the prior art, not in applicant's disclosure."). "Obviousness does not require absolute predictability, but a reasonable expectation of success is necessary." In re Clinton, 527 F.2d 1226, 1228, 188 U.S.P.Q. 365, 367 (C.C.P.A. 1976).

Applicants submit that Goon et al. does not provide the requisite expectation of success. Applicants repeat again what is recited in Goon i.e. [t]he introduction of a fluorohexose or hexosamine analog into a biosynthetic pathway *might* lead to metabolic *incorporation* or metabolic *disruption* (emphasis added). Furthermore, obvious to try a modification represents an insufficient basis to modify or combine references. In moving from the prior art to the claimed invention, one cannot base a determination of obviousness on what the skilled person might try or find obvious to try. Rather, the proper test requires determining what the prior art would have led the skilled person to *do*.

In *In re Tomlinson*, 363 F.2d 928, 150 U.S.P.Q. 623 (C.C.P.A. 1966), the CCPA considered the patentability of an invention directed to polypropylene stabilized with a particular class of dithiocarbamates. The prior art disclosed polyethylene stabilized with these dithiocarbamate compounds. Because of the close structural similarity between polypropylene and polyethylene, the PTO concluded that a skilled chemist would have found it obvious to try to stabilize polypropylene with a known stabilizer for polyethylene. The court responded to the PTO's position on this matter by noting that "there is usually an element of 'obviousness to try' in any research endeavor, that it is not undertaken with complete blindness but rather with some semblance of a chance of success." *Id.* at 931, 150 U.S.P.Q. at 626. Permitting patentability determinations based on an "obvious to try" test "would not only be contrary to statute but result in a marked deterioration of the entire

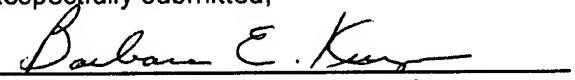
patent system as an incentive to invest in those efforts and attempts which go by the name of 'research.'" *Id.*

The Federal Circuit has given some examples of what would constitute an "obvious to try" modification based on the prior art. See *In re O'Farrell*, 853 F.2d 894, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988). "In some cases, what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was 'obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." *Id.* at 903, 7 U.S.P.Q.2d at 1681 (citations omitted).

Goon et al. does not give any indication of which parameters are critical to the modification of compounds disclosed in Ohsumi et.al. i.e. the parameters critical to providing fluorine-substituted compounds that had substantially similar or better inhibitory activity against SGLTs.

Claim 8 has been canceled via the instant amendment. In view of the arguments herein, Applicants respectfully request that the rejection of Claims 1-7 be withdrawn.

Respectfully submitted,



Barbara E. Kurys, Reg. No.: 34,650
Attorney/Agent for Applicant

sanofi-aventis U.S. Inc.
U.S. Patent Operations
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807-0800
Telephone (908) 231-**2965**
Telefax (908) 231-2626

sanofi-aventis Docket No. DEAV2002/0087 US NP